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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,948	12/04/2006	Yukio Sato	P28700	6527

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
01/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,948	SATO ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/4/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

2. The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

3. The information disclosure statement filed on 12/4/2006 has been considered. An initialed copy is enclosed.

Claim Objections

4. Claims 5-9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 is drawn to a pharmaceutical composition comprising the polynucleotide of claim 1 as an active ingredient. Claim 6 is drawn a pharmaceutical composition of claim 5 which is a pharmaceutical composition for preventing and/or treating immune-disease mediated diseases. Claim 7 is drawn to a pharmaceutical composition of claim 5 which is an immunosuppressive agent. Claim 8 is drawn to a pharmaceutical composition of claim 5 which is an agent for treating arthritis. Claim 9 is drawn to an agent for suppressing generation of interleukin. Claims 5 and 7 does not further limit claim 1 because a polynucleotide comprising a CpG motif inherently is an active ingredient and an immunosuppressive agent. Claims 6, 8 and 9 does not further limit claim 1 because a polynucleotide comprising a CpG motif for preventing and or treating immune-mediated

diseases, treating arthritis, and for suppressing generation of interleukin is considered an intended use and thus is given no patentable weight on the composition.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising CMG-DNA for treating arthritis and for mCG-DNA and CMG-DNA to suppress and enhance the induction of IL-6 does not provide enablement a pharmaceutical composition for preventing and or treating all immune mediated disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;

(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention. The claims are drawn to the composition of claim 5 which is a pharmaceutical composition for preventing and/or treating immune mediated disease.

The breadth of the claims. The product being used for the prevention and treatments of all immune mediated diseases is overly broad. drawn to the composition of claim 5 which is a pharmaceutical composition for preventing and/or treating immune mediated disease. The quantity of experimentation required to practice the invention as claimed would require the determination of accessible target sites, modes of delivery and formulations, the route and time course of administration that encompass the composition of claim with limitations as discussed above to target appropriate cells and/or tissues in any and/or all organisms/subjects, and further whereby treatment effects are provided for the claimed conditions. Therefore it is hard for one skilled in the art to determine if the composition can be used for the prevention and treatments of all immune mediated diseases in a subject (human or otherwise). Since the specification fails to provide particular guidance for treating any subject with all immune-mediated diseases with the composition of claim 5 which is a pharmaceutical composition for preventing and/or treating immune mediated disease it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Guidance of the specification/The existence of working examples: The specification discloses examples of in vitro treatment using mCG-DNA and CMG-DNA

to suppress and enhance the induction of IL-6 (see example 1). The specification discloses an examples of in vivo treatment using CMG-DNA to treat arthritis (see example 2). Furthermore, Applicants have not provided guidance in the specification toward the pharmaceutical composition preventing immune mediated diseases. Therefore, the specification as filed fails to provide particular guidance demonstrating a reasonable extrapolation which resolves the known unpredictability in the art associated with preventing and or treating all types of immune/mediated disease, in any and/or all organisms whereby treatment effects are provided in any and/or all organisms. The skilled artisan would clearly realize the critical deficiency of this specification with respect to prevention and or treatment of immune diseases.

The state of the prior art. The state of the art is unpredictable with to a pharmaceutical composition of claim 5 for preventing and or treating immune-mediated disease. The art indicates the use of a methylated CpG ODN 1812, which is identical to ODN 1758 that had little effect (see Weiner et al 1997 Proc. Natl. Acad. Sci. USA Vol. 94 pgs. 10833-10837 especially pgs. 10834-10836). The art indicates that CpG oligonucleotides are useful and can act as adjuvants to induce cytokine production (see Chu et al 1997 CpG Oligodeoxynucleotides Act as Adjuvants that Switch on T Helper 1 (TH1) Immunity pgs. 1623-1630 in its entirety). CpG-ODNs have multiple stimulatory effects on lymphocytes, including macrophages, B cells, natural killer (NK) cells and T cells (see Goldberg et al 2000 Immunology Letters.73:13-18 in its entirety and especially on p. 14). The art indicates that methylated DNA does not induce cytokine production in spleen cells from a murine model (see Krieg et al US Patent No: 6,653,292B1 Date Nov. 25, 2003 column 20 lines 15-25Table 3). The state of the art questions whether CpG containing oligonucleotides can treat preexisting tumor in the animal model (see Katoaka et al (Jpn. J. Cancer Res. 1992 Vol. 83 pgs. 244-247). The art acknowledges the importance of Thl type immune response, which is stimulated by the production of Thl associated Cytokines, in the elimination of intracellular pathogens, including viruses. However, the art has not accredited or recognized any one particular Thl-associated cytokine to the

treatment, prevention and amelioration of viral infection in a subject. Specifically, the art teaches that while cytokines secreted by T helper cells are of critical importance for the outcome of many infectious diseases, the production of the "right" set of cytokines can be a matter of life or death, as noted by Infante-Duarte et al. Infante-Duarte et al. further notes that in addition to a Thl type immune response, a Th2 type immune response is also necessary. Specifically, Infante-Duarte et al. teaches that a tight control over where and when Thl and Th2 immune responses happen is necessary to keep intracellular infections under control, and to prevent the Thl type immune response from causing damage to the host.1 Hence, while the importance of a Thl type immune response is well recognized in the art, the art further notes that a balance between Thl and Th2 type immune responses is necessary to resolve an infection (Infante-Duarte et al., Thl/Th2 balance in infection. Springer Seminars in Immunopathology, 1999, 21: 317-338). [Paragraph bridging pages 321-322, in particular.]. The state of the art shows that there are limitations in prevention and or treating immune-mediated diseases. For the reasons set forth supra, the state of the art is unpredictable for treating and preventing all types of immune mediated diseases.

In conclusion, the claimed invention is not enabled for the pharmaceutical composition of claim 5 for preventing and or treating immune mediated diseases. The claims are drawn to the composition of claim 5 which is a pharmaceutical composition for preventing and/or treating immune mediated disease. The specification fails to teach a pharmaceutical composition for preventing immune mediated diseases. There is a lack of working examples. The state of the art shows that there are limitations in prevention and or treating immune-mediated diseases. In view of the lack of support in the art and specification for an effective composition of the claimed invention, it would require undue experimentation on the part of the skilled artisan to make and use the composition as claimed; therefore the claim is not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg et al WO 98/1880 Date May 7, 1998.

Claims 1-9 are drawn to a polynucleotide a polynucleotide comprising a CpG motif wherein guanine is methylated.

Krieg et al teach SEQ ID NO: 1 (see STIC RESULTS). Krieg et al teach methylated oligonucleotides (polynucleotide) comprising a CpG motif, wherein the length is 8 to 100 nucleotides.

Krieg does not teach

Krieg et al further teach a pharmaceutical composition which comprises an oligonucleotide (polynucleotide) as an active ingredient, a pharmaceutical composition for preventing and/or treating immune-mediated diseases. Krieg et al further teach a pharmaceutical composition which is an immunosuppressive agent, wherein an agent is an agent for treating arthritis. Krieg et al further teach an agent for suppressing generation of interleukin which comprising an oligonucleotide (polynucleotide) as an active ingredient (see Krieg et al in its entirety).

It would have been prima facie obvious at the time the invention was made to produce a polynucleotide as taught by Krieg et al and to modify a polynucleotide comprising a CpG motif wherein guanine is methylated as taught by Krieg et al because Krieg et al teach methylated oligonucleotide for preventing and/or treating immune-mediated diseases, treating arthritis, and as an agent for suppressing generation of interleukin.

Status of the Claims

7. No claims are allowed.

Claims 1-9 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER